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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
**K. KATAGAI, et al.**

Serial No.: **Corresponding to PCT/JP99/06241 filed November 10, 1999**

Filed: **Concurrently Herewith**

For: **Adhesive Gel Compositions For Iontophoresis And Devices Therefor**

**TRANSMITTAL OF ENGLISH TRANSLATION OF AMENDMENTS FILED UNDER PCT ARTICLE 34**

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

Attached hereto are English translations of an Amendment filed June 7, 2000 (Substituted page for original page 61); and Amendment filed October 5, 2000 (Substituted pages for the original pages 5, 35 and 60), made to the international application pursuant to Article 34 entitled "Procedure Before the International Preliminary Examining Authority".

Respectfully submitted,

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disclosed in JP-A-63-92683 also involves a problem due to the fact that it should contain an increased amount of a base polymer for enabling a plastering because of its low viscosity upon plastering and that such base polymer should be neutralized with an alkali. Accordingly, with such conventional hydrophilic adhesive composition, an increase in the diffusion resistance of a drug or a reduction in the delivery rate is caused, resulting in a problem of a substantial reduction in the permeability of the drug.

While each of a base consisting of a copolymer of acrylic acid and acrylamide disclosed in JP-A-5-97662 and an adhesive composition consisting of a methoxymaleic anhydride copolymer or a methoxy maleic acid copolymer and an N-vinylacetamide crosslinked structure disclosed in JP-A-9-286891 undergoes no deterioration of the characteristics such as an adhesive performance upon addition of a neutral electrolyte or component, it allows the absorption to be reduced due to a reduction in the solubility of a drug in case of the addition of a component which causes the pH of the gel such as a basic drug. Also when an acidic pH modifier such as hydrochloric acid is added for suppressing the change in the pH of a gel, there is a problem that the moldability and the adhesive performance of the gel are reduced.

Accordingly, an object of the present invention is to solve the problems described above and to provide an adhesive

| | |
|---|---|
| Epinephrine | 0.1 Part by weight |
| Sodium hydrogen sulfite | 0.3 Part by weight |

These components in the above formulation were mixed and stirred with heating at 50°C until a uniform mixture was obtained, and epinephrine, an antioxidant and a crosslinking agent were added finally at 40°C to obtain a comparative adhesive composition. The composition was plastered onto a release-treated PET liner to have a thickness of 1 mm, and cut into a suitable form and subjected to a test.

(Comparative Example 6)

| | |
|---|---|
| Polyacrylic acid | 6 Parts by weight |
| Glycerin | 40 Parts by weight |
| Aluminum hydroxide | 1 Part by weight |
| Gelatin | 5 Parts by weight |
| Water | 39.6 Parts by weight |
| Lidocaine | 8 Parts by weight |
| Epinephrine | 0.1 Part by weight |
| Sodium hydrogen sulfite | 0.3 Part by weight |

These components in the above formulation were mixed and stirred with heating at 50°C until a uniform mixture was obtained, and epinephrine, an antioxidant and a crosslinking agent were added finally at 40°C to obtain a comparative adhesive composition. The composition was plastered onto a release-treated PET liner to have a thickness of 1 mm, and cut into a suitable form and subjected to a test.

ART 34 AMDT

What is claimed is:

1. (Amended) An adhesive gel composition for an iontophoresis comprising (a) basic drug(s), an acidic polymer (except methoxyethylene maleic anhydride copolymer and methoxyethylene maleic acid copolymer), a polyfunctional epoxy compound, water, a polyhydric alcohol and/or a gelatin.

2. An adhesive gel composition for an iontophoresis according to Claim 1 wherein the weight ratio of the basic drug(s) to the acidic polymer is 10:1 to 1:10.

3. An adhesive gel composition for an iontophoresis according to Claim 1 or 2 wherein the acidic polymer is one or more selected from the group consisting of a polyacrylic acid, a methoxyethylene maleic anhydride copolymer, a methoxyethylene maleic acid copolymer, an isobutylene maleic anhydride copolymer, an isobutylene maleic acid copolymer, a carboxyvinyl polymer and carboxymethyl cellulose.

4. An adhesive gel composition for an iontophoresis according to any of Claims 1 to 3 wherein at least one of the basic drug(s) is(are) in a free form.

5. An adhesive gel composition for an iontophoresis according to Claim 4 wherein the basic drug is a local anesthetic agent.

6. An adhesive gel composition for an iontophoresis according to Claim 4 wherein the basic drugs are a local anesthetic agent and a vasoconstrictor.

7. An adhesive gel composition for an iontophoresis according to Claim 6 wherein the local anesthetic agent is lidocaine and the vasoconstrictor is epinephrine.

8. An adhesive gel composition for an iontophoresis according to Claim 7 wherein the weight ratio of lidocaine to epinephrine is 1000:1 to 2:1.

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9. An adhesive gel composition for an iontophoresis according to Claim 7 comprising 1 to 20 % by weight of lidocaine and 0.001 to 0.5 % by weight of epinephrine.

10. An adhesive gel composition for an iontophoresis according to Claim 7 further comprising an antioxidant.

11. An adhesive gel composition for an iontophoresis according to Claim 10 wherein the antioxidant is one or more selected from the group consisting of sodium pyrosulfite, sodium hydrogen sulfite and oxyquinoline sulfate.

12. An adhesive gel composition for an iontophoresis according to Claim 10 or 11 comprising 0.001 to 1.0 % by weight of an antioxidant.

13. (Amended) An iontophoresis device comprising a donor electrode, a donor electrode-side composition arranged on the donor electrode, a reference electrode, a reference electrode-side composition arranged on the reference electrode and a power supply connected electrically to each of the donor electrode and the reference electrode, wherein the donor electrode-side composition contains any of the adhesive gel compositions for an iontophoresis according to Claims 1 to 12; wherein the current output from the source device is at least one of a direct current, a pulse direct current and a pulse depolarized direct current and wherein the current rate is 0.25 to 5.00 $mA \cdot min/cm^2$.